

WE CLAIM:

1. A method of identifying a modulator of chondrogenesis comprising:
- 5 (a) providing cells capable of differentiating into chondroblasts or chondrocytes;
- (b) transfecting the cells with a nucleic acid construct comprising a reporter gene that is detectable upon chondroblast or chondrocyte differentiation;
- 10 (c) adding a test compound to the transfected cells; and
- (d) determining the effect of the test compound on chondroblast or chondrocyte differentiation.
2. A method according to claim 1 wherein the cells are mesenchymal cells.
- 15 3. A method according to claim 1 wherein the cells are limb mesenchymal cells.
4. A method according to claim 1 wherein the reporter gene encodes an enhancer element that binds to a transcription factor whose activity changes during chondroblast differentiation.
- 20 5. A method according to claim 4 wherein the reporter gene is responsive to the transcription factor Sox9.
- 25 6. A method according to claim 5 wherein the nucleic acid construct comprises at least one Sox9 binding site, a promoter and a detectable marker.
- 30 7. A method according to claim 6 wherein the nucleic acid construct contains four Sox9 binding sites.

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8. A method according to claim 6 wherein the marker encodes a luciferase or an enhanced green fluorescent protein.

9. A method according to claim 6 wherein the nucleic acid construct is
5 pGL3(4X48)-luciferase as shown in Figure 6.

10. A method according to claim 6 wherein the nucleic acid construct is pGL3(4X48)-enhanced green fluorescent protein as shown in Figure 6.

10 11. A method according to claim 1 wherein the transfection is a transient transfection.

SVB A2 12. A method according to claim 1 wherein the cells are plated at high density.

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13. A method according to claim 1 wherein the test compound is a nucleic acid molecule comprising a test gene that is transfected into the cells.

14. A nucleic acid construct which is pGL3(4X48)-luciferase as shown in
20 Figure 6.

15. A nucleic acid construct which is pGL3(4X48)-enhanced green fluorescent protein as shown in Figure 6.

25 16. A kit for identifying modulators of chondrogenesis comprising a nucleic acid construct comprising a reporter gene that is responsive to the transcription factor Sox9 and instructions for the use thereof.

17. A kit according to claim 16 comprising the nucleic acid construct pGL3
30 (4X48)-luciferase as shown in Figure 6.

18. A kit according to claim 16 comprising the nucleic acid construct pGL3 (4X48)-enhanced green fluorescent protein as shown in Figure 6.

19. A method of diagnosing or monitoring a disease that is associated with a modulation in chondrogenesis comprising:

- (a) providing cells capable of differentiating into chondroblasts or chondrocytes;
- (b) transfecting the cells with a nucleic acid construct comprising a reporter gene that is detectable upon chondroblast or chondrocyte differentiation;
- (c) adding a test sample to the transfected cells; and
- (d) determining the effect of the test sample on chondroblast or chondrocyte differentiation.

20. A method according to claim 19 wherein the test sample is a bodily fluid.

21. A method according to claim 19 wherein the bodily fluid is synovial fluid.

22. A method of conducting a drug discovery business comprising:

- (a) providing one or more assay systems for identifying a modulator of chondrogenesis;
- (b) conducting therapeutic profiling of modulators identified in step (a), or further analogs thereof, for efficacy and toxicity in animals; and
- (c) formulating a pharmaceutical preparation including one or more modulators identified in step (b) as having an acceptable therapeutic profile.

23. A method of conducting a target discovery business comprising:

- 5 (a) providing one or more assay systems for identifying modulators of chondrogenesis;
- (b) (optionally) conducting therapeutic profiling of modulators identified in step (a) for efficacy and toxicity in animals; and
- (c) licensing, to a third party, the rights for further drug development and/or sales for modulators identified in step (a), or analogs thereof.

10 24. A modulator of chondrogenesis identified according to the method of claim 1.

15 25. A pharmaceutical composition for use in the modulation of chondrogenesis comprising a modulator of chondrogenesis identified according to the method of claim 1.

26. A method of making a pharmaceutical composition for use in modulating chondrogenesis comprising mixing a modulator of chondrogenesis identified according to a method of claim 1 with a suitable diluent or carrier.

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